FORM PTO-1390 (Modified) (REV 11-2000) U S DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371

ATTORNEY'S DOCKET NUMBER: **RLL-165US**

U S APPLICATION NO (IF KNOWN, SEE 37 CFR): HEREWITH 09/936934

INTERNATIONAL APPLICATION NO	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/IB99/01735	**OCTOBER 26, 1999**	**MARCH 19, 1999**

TITLE OF INVENTION
TASTE MASKING COATING COMPOSITIONS

APPLICANT(S) FOR DO/EO/US
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Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information

1. ☒ This is a **FIRST** submission of items concerning a filing under 35 U S.C. 371.
2. ☐ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U S C. 371.
3. ☒ This is an express request to begin national examination procedures (35 U.S C 371(f)). The submission must include items (5), (6), (9) and (24) indicated below.
4. ☒ The US has been elected by the expiration of 19 months from the priority date (Article 31).
5. ☒ A copy of the International Application as filed (35 U.S.C. 371 (c) (2))
   a. ☐ is attached hereto (required only if not communicated by the International Bureau).
   b. ☒ has been communicated by the International Bureau
   c. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US).
6. ☐ An English language translation of the International Application as filed (35 U.S.C. 371(c)(2)).
   a. ☐ is attached hereto.
   b. ☐ has been previously submitted under 35 U.S C 154(d)(4).
7. ☒ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371 (c)(3))
   a. ☐ are attached hereto (required only if not communicated by the International Bureau).
   b. ☐ have been communicated by the International Bureau.
   c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
   d. ☒ have not been made and will not be made.
8. ☐ An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
9. ☐ An oath or declaration of the inventor(s) (35 U.S.C. 371 (c)(4)).
10. ☐ An English language translation of the annexes of the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371 (c)(5)).
11. ☐ A copy of the International Preliminary Examination Report (PCT/IPEA/409).
12. ☒ A copy of the International Search Report (PCT/ISA/210).

Items 13 to 20 below concern document(s) or information included:

13. ☐ An Information Disclosure Statement under 37 CFR 1.97 and 1 98
14. ☐ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
15. ☐ A **FIRST** preliminary amendment.
16. ☐ A **SECOND** or **SUBSEQUENT** preliminary amendment.
17. ☐ A substitute specification.
18. ☐ A change of power of attorney and/or address letter
19. ☐ A computer-readable form of the sequence listing in accordance with PCT Rule 13ter.2 and 35 U.S C 1.821 - 1 825.
20. ☐ A second copy of the published international application under 35 U S C. 154(d)(4).
21. ☐ A second copy of the English language translation of the international application under 35 U S.C 154(d)(4).
22. ☒ Certificate of Mailing by Express Mail
23. ☒ Other items or information:

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U.S. APPLICATION NO (IF KNOWN, SEE 37 CFR HEREWITH)	INTERNATIONAL APPLICATION NO	ATTORNEY'S DOCKET NUMBER
09/936934	PCT/IB99/01735	RLL-165US

24. The following fees are submitted..	CALCULATIONS PTO USE ONLY	
BASIC NATIONAL FEE (37 CFR 1.492 (a) (1) - (5)) :		
☐ Neither international preliminary examination fee (37 CFR 1 482) nor international search fee (37 CFR 1 445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO **$1000.00**		
☐ International preliminary examination fee (37 CFR 1 482) not paid to USPTO but International Search Report prepared by the EPO or JPO **$860.00**		
☐ International preliminary examination fee (37 CFR 1 482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO **$710.00**		
☒ International preliminary examination fee (37 CFR 1 482) paid to USPTO but all claims did not satisfy provisions of PCT Article 33(1)-(4) **$690.00**		
☐ International preliminary examination fee (37 CFR 1.482) paid to USPTO and all claims satisfied provisions of PCT Article 33(1)-(4) . **$100.00**		
ENTER APPROPRIATE BASIC FEE AMOUNT =	**$690.00**	
Surcharge of **$130.00** for furnishing the oath or declaration later than ☐ 20 ☒ 30 months from the earliest claimed priority date (37 CFR 1 492 (e))	**$130.00**	

CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE		
Total claims	14 - 20 =	0	x $18.00	**$0.00**	
Independent claims	1 - 3 =	0	x $80.00	**$0.00**	
Multiple Dependent Claims **(check if applicable).**			☐	**$0.00**	
TOTAL OF ABOVE CALCULATIONS =				**$820.00**	
☐ Applicant claims small entity status. (See 37 CFR 1.27). The fees indicated above are reduced by 1/2.				**$0.00**	
SUBTOTAL =				**$820.00**	
Processing fee of **$130.00** for furnishing the English translation later than ☐ 20 ☐ 30 months from the earliest claimed priority date (37 CFR 1 492 (f)). +				**$0.00**	
TOTAL NATIONAL FEE =				**$820.00**	
Fee for recording the enclosed assignment (37 CFR 1 21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31) **(check if applicable).** ☐				**$0.00**	
TOTAL FEES ENCLOSED =				**$820.00**	
				Amount to be: refunded	$
				charged	$

a. ☐ A check in the amount of _____ to cover the above fees is enclosed.

b. ☒ Please charge my Deposit Account No. **50-0912** in the amount of **$820.00** to cover the above fees. A duplicate copy of this sheet is enclosed

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d. ☐ Fees are to be charged to a credit card **WARNING:** Information on this form may become public **Credit card information should not be included on this form.** Provide credit card information and authorization on PTO-2038.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO

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34,507

REGISTRATION NUMBER

SEPTEMBER 19, 2001

DATE

TASTE MASKING COATING COMPOSITIONS

FIELD OF THE INVENTION

The present invention relates to a coating composition effective for taste masking of bitter and unpalatable drugs.

BACKGROUND OF THE INVENTION

Most prescription and non-prescription drugs are administered orally as tablets or capsules. However, patients at the extremes of age, such as children and the elderly, often experience difficulty in swallowing such solid dosage forms. For such patients drugs can be provided either as chewable or dispersible tablets or, as liquid dosage forms such as solutions, emulsions and suspensions. These dosage forms permit perceptible exposure of the active drug to the taste buds. Some drugs are extremely bitter and therefore unpalatable when given in these dosage forms. As a consequence, measures need to be taken to mask the taste of these drugs in order to enhance patient compliance.

Several techniques to make liquid dosage forms palatable, are reported in the literature. These include the use of relatively insoluble salts of the parent drug resulting in lower exposure of the drug in perceptible form in the mouth. Syrups with or without flavouring, are often sufficient to mask the taste of drugs. However, some drugs have such a pronounced bitterness that conventional approaches such as the use of sweetners, amino acids, flavors and adsorbents are unsuccessful. This is particularly problematic if the drug in question is extensively used in treating children or the elderly. There is, therefore, a need to develop approaches that would be effective in masking the taste of bitter drugs.

US 4,808,411 describes a taste masked pharmaceutical composition comprising erythromycin or its derivatives and a carbomer. The drug-polymer complex is believed to be held together by ionic attraction between the amine group of erythromycin compound and carbonyl group of the carbomer, and by the gel properties of the insoluble carbomer. This provides for a minimal dissolution of the erythromycin compound in a non-ionic aqueous medium, so that the drug is released from the complex slowly enough to avoid a significant perception of bitterness in the mouth. In the gastro-intestinal tract, the ionic environment causes liberation of the erythromycin compound. Thus, by controlling the availability of the drug in the free form, taste masking of the drug is achieved. This method, however, will be useful for masking the taste of only those drugs which can form reversible complexes and will, therefore, be limited in its utility.

US 4,865,851 describes a taste masked formulation of cefuroxime axetil where the drug particles are provided with integral coatings of a lipid or mixtures of lipids which are insoluble in water and which serve to mask the bitter taste of cefuroxime axetil upon oral administration. This coating however, results in a significant reduction in the dissolution and consequently the bioavailability of cefuroxime axetil suspension is significantly low as compared to tablet dosage form.

US 5,695,784 describes a method for taste masking of bitter drugs where the coating composition comprises a cationic copolymer of dimethylaminoethyl methacrylate and neutral methacrylate acid esters, neutral methyl esters and/or ethyl ester compounds of polymethacrylic acid, quaternary ammonium compounds of

polymethacrylic acid or ethylcellulose and triethylcitrate and optionally hydroxypropyl methylcellulose. This coating composition requires the application of large quantities of polymers for effective taste masking.

SUMMARY OF THE INVENTION

The present invention describes coating compositions and processes for the preparation of a pharmaceutical coating composition, effective in masking the taste of medicinal compounds, to be applied over the core constituted of medicinal compound. The core may comprise primary drug particles, granules, crystals, pellets or even unit dosage forms like tablets. The coat comprises a film forming polymer and a high viscosity swellable polymer, optionally also including other suitable ingredients for coating including lubricants, plasticizers and channeling agents.

The combination of film forming polymer with swellable polymer imparts in the film a barrier property for the control of initial drug release suitable for taste-masking, without compromising on drug release over the stipulated duration of a conventional, immediate release formulation. For very bitter drugs polymer applications may be as high as 80% on fine cores using conventional coating polymers. The present composition is capable of achieving the same degree of taste masking in as little as 10 to 15% of polymer application, equivalent to 20 - 30% of total solids applied. This, therefore, results in uniformity of coating thickness, process reproducibility, faster rate of dissolution and uncompromised bioavailability. It also makes the process cost effective and less time consuming.

A variety of polymeric materials can be employed for film forming. Non-limiting examples of such film forming polymers may belong to the class of acrylic polymers, cellulosic polymers or vinyl polymers. The acrylic polymers used will be those available under the trade name Eudragit® from Rohm Pharma. More preferably the acrylic polymers may be methacrylic acid co-polymers sold under the trade name Eudragit L® and Eudragit S®, and polyethylacrylate-methylmethacrylate sold under the trade name, Eudragit NE®.

Cellulosic film-forming agents which are useful, include, alkylcelluloses, such as, methyl or ethyl cellulose and, hydroxyalkylcelluloses (eg., hydroxypropylcellulose or hyroxypropylmethyl-celluloses). The alkyl cellulosic film forming polymers include those sold under the trade names Methocel E™ and Surelease by Dow Chemicals, and Aquacoat® of FMC. Examples of vinyl film forming polymers include polyvinyl acetate or polyvinyl acetate pthalate. The dry weight of the film forming polymer may be applied to a maximum of 30% of the weight of the core for taste masking.

The swellable polymers which may be used in combination with the film forming polymers include carbopol, high viscosity gums, carrageenan, high viscosity vinyl polymers or high viscosity cellulosic polymers such as Methocel™ K series polymers (Trademark Dow Chemicals). Swellable polymers may be present from 0.1 - 20% of the dry weight of film forming polymer.

The coating composition may optionally include pharmaceutically acceptable excipients, which are conventionally used as a channeling agent such as starch, lactose or (PEG) poly ethylene glycol. The channeling agent may be present upto

100%, preferably 60%, or more preferably, upto 30% of the dry weight of the film forming polymer.

The coating composition also contains lubricants which function as anti-sticking agents (e.g. talc, colloidal silica and magnesium stearate) and pharmaceutically acceptable plasticisers (e.g. triethyl citrate, polyethylene glycol, glyceryl monostearate, glyceryl triacetate, acetyl triethylcitrate, triethylcitrate, dibutyl phthalate and dibutyl sebacate). The lubricant quantity may be upto 200% of the dry weight of film-forming polymer, and more preferably, upto 100% of the dry weight of the film-forming polymer. The plasticiser quantity may be upto 40% the dry weight of the film forming polymer. The coated formulations may optionally be cured at elevated temperatures.

A total polymer content in the coating of upto 30% by weight of pharmaceutical cores or, more preferably, 10% by weight of pharmaceutical cores is sufficient to mask the taste of bitter tasting, highly water soluble drugs.

The taste masked coated particles obtained by the composition of the present invention, can be mixed with food or beverages, can be used to prepare liquid suspensions for oral administration, or can be formulated into conventional whole, chewable, or dispersible tablets for oral administration. In forming tablets or liquid suspensions, pharmaceutically acceptable ingredients well known in conventional arts can be employed. For use in suspensions, a mean average particle size of less than 50 mesh (297 microns) is preferred. The drug may optionally be first formulated as pellets, tablets or capsules, which may then be coated for taste-masking.

The examples given herein further illustrate the invention and are not intended to limit the scope of the invention:

DETAILED DESCRIPTION OF THE INVENTION

EXAMPLE 1

Table 1.1 shows a coating composition which has been used for taste masking of a number of drug cores :

Table 1.1

Ingredient	Amount used (g)	Dry wt. (g)
Eudragit L30D	333.33	100.0
Carbomer (Aqueous Carbopol® 971P Dispersion 1% w/w)	200.0	2.0
Talc USP (Aqueous Talc Dispersion 30% w/w)	40.80	102.0
Polyethylene glycol USNF (PEG 1500)	15.3	15.3
Purified Water USP upto..	1000.00	-

To prepare the coating solution, an aqueous talc dispersion (30% w/w), was added to a 1% w/w carbopol dispersion in water under stirring for 30 minutes.

Carbopol-talc dispersion was finally added into plasticized (with PEG 1500) Eudragit dispersion with stirring for 30-40 minutes.

Procedure for preparation of core particles :

Table 1.2

Ingredient	Amount used (g)
Norfloxacin USP	260.0
Microcrystalline Cellulose USNF (Avicl® PH 102)	88.0
Pregelatinized Starch USNF (Sarch 1500)	10.0
Povidone USP (PVP K-30)	30.0
Colloidal Silicon Dioxide USNF (Aerosil® 200)	2.0
Magnesium Stearate USNF	0.75

Weighed amount of ingredients (except Aerosil 200) were sifted through British Standard Sieve (BSS) #44 and mixed for 10 minutes in a double cone blender, followed by the addition of Aerosil 200 (sifted through BSS #60) and an additional mixing of 2 minutes. The blend was then granulated with water and dried at 60°C in a tray-drier for 24 hours. The granules obtained were sifted to give (BSS)# 44 / #85 fraction.

Resultant granules (150g) were lubricated with 0.5% magnesium stearate and sprayed with the prepared coating solution using Wurster coater (Glatt GPCG-1 from Glatt GmbH, Germany). The total polymer content of the applied coat was 12.0% by weight of the core while the total solids applied was 26% by weight of the core. A total polymer coating of only 12% was sufficient to mask the bitter taste of Norfloxacin while giving optimum dissolution required for immediate release formulations. (Table 1.3).

Table 1.3

Time (Min.)	Percent drug released USP Buffer pH 4.0; 50rpm; 900ml	
	Uncoated	Coated
5	63.80	2.30
10	95.73	19.40
15	106.40	38.30
20	--	54.23
25	--	66.37
30	--	82.17

EXAMPLE 2

In this example, ibuprofen was granulated and coated for taste masking, as discussed below.

Table 2.1

Ingredient	Amount used (g)
Ibuprofen USP	260.0
Microcrystalline Cellulose (Avicel® PH 102)	88.0
Pregelatinized Starch USNF (Starch 1500)	10.0
Povidone USP (PVP K-30)	30.0
Colloidal Silicon Dioxide USNF (Aerosil® 200)	2.0
Magnesium Stearate USNF	0.75

Weighed amounts of Ibuprofen, Avicel 102, Starch 1500 and PVP K-30 were sifted through BSS #44 and mixed for 10 mins. in a double cone blender. Aerosil 200 was sifted through BSS #60 and added to the blend in the double cone blender and mixed for an additional 2 minutes. The blend was granulated with water and dried at 60°C in a tray drier for 4 hours. After sifting through BSS #44 and BSS #85, the #44/85 fraction (150gm) was lubricated with magnesium stearate (0.75g). The dried and lubricated granules (150.0g) were sprayed with the prepared coating solution as described in Example 1(Table 1.1). Only a 6% coating of polymers by weight of the core (total solids applied was 13%) was sufficient to mask the taste of ibuprofen. Coated granules when kept in the mouth for 1-2 minutes, did not give any bitter taste. The dissolution of ibuprofen was not significantly affected by this coat, as shown in the Table 2.2.

Table 2.2

Time (Min.)	Percent drug released Phosphate Buffer pH 7.2; 150rpm; 900ml	
	Uncoated	Coated
5	54.30	46.27
10	85.63	76.03
15	94.06	88.97
20	97.00	93.37
25	97.40	93.00
30	97.90	94.70

EXAMPLE 3

Table 3.1

Ingredient	Amount used (g)
Etodolac BP	200.0
Microcrystalline Cellulose USNF (Avicel® PH 102)	148.0
Pregelatinized Starch USNF (Starch 1500)	10.0
Povidone USP (PVP K-30)	30.0
Colloidal Silicon Dioxide USNF (Aerosil® 200)	2.0
Magnesium Stearate USNF	0.75

Etodolac, Avicel PH 102, Starch 1500 and PVP K-30 were blended in a double cone blender. Aerosil 200, sifted through BSS #60, was added to the blend and mixed for 2 minutes. The blend was granulated with water and dried at 60°C for 4 hours. Dried material was sifted to obtain fraction of BSS #44/85 and lubricated with magnesium stearate (0.75g). The dried and lubricated granules (150.g) were sprayed with the prepared coating solution as described in Example 1 (Table 1.1). The total polymer coating of 12.0% by weight of the core was sufficient to mask the bitter taste of the drug. The total solids applied was 26%. The coated granules gave optimum dissolution as shown in Table 3.2.

Table 3.2

Time (Min.)	Percent drug released Phosphate Buffer pH 7.5; 100rpm; 900ml	
	Uncoated	Coated
5	86.60	29.70
10	91.37	73.10
15	93.43	88.00
20	94.00	92.80
25	--	94.40
30	--	94.90

EXAMPLE 4

Table 4.1

Ingredient	Amount used (g)
Paracetamol USP	260.0
Microcrystalline Cellulose USNF (Avicel® PH 102)	88.0
Pregelatinized Starch USNF (Starch 1500)	10.0
Povidone USP (PVP K-30)	30.0
Colloidal Silicon Dioxide USNF (Aerosil® 200)	2.0
Magnesium Stearate upto	0.75

Paracetamol, Avicel PH 102, Starch 1500 and PVP K-30 were blended in double cone blender. Aerosil 200 was sifted through BSS #60 and blended for 2 minutes. The blend was granulated with water and dried at 60°C for 4-5 hours. 150 g of the dried fraction (BSS #44/85) was lubricated with magnesium stearate (0.75 g). The dried and lubricated granules (150g) were sprayed with the prepared coating solution as described in Example 1 (Table 1.1). The total polymer and solids applied were 8% and 17.5% by weight of the core, respectively which was sufficient to mask the taste of the drug without affecting the dissolution (Table 4.2).

Table 4.2

Time (Min.)	Percent drug released Phosphate Buffer pH 5.8; 50rpm; 900ml	
	Uncoated	Coated
5	76.10	61.90
10	96.30	86.60
15	96.90	92.60
20	97.00	94.10
25	97.40	94.40
30	--	94.90

EXAMPLE 5

Table 5.1

Ingredient	Amount used (g)
Ciprofloxacin Hydrochloride USP (equivalent to 200g Ciprofloxacin USP)	239.0
Hydroxypropyl Cellulose USNF (HPC-L)	11.2
Colloidal silicon dioxide USNF (Aerosil® 200)	0.75

Microcrystalline cellulose USNF, (Celphere®)	100.0
Talc USP (Aqueous Talc Dispersion 30% w/w)	14.0
Purified Water USP upto	670.0

A dispersion was pepared by dissolving HPC-L in water, followed by the addition of ciprofloxacin hydrochloride and talc with vigorous stirring. The suspension was homogenised for 30 minutes, sieved and coated on 100 g microcrystalline cellulose spheres (Celphere® , FMC Corp., USA) having an average particle size of 170μm.

Procedure for layering : Celphere beads (100 g) were introduced into the processing chamber of Wurster coater (Glatt GPCG-1 from Glatt GmbH, Germany) and the prepared drug suspension was sprayed from the bottom at a spray rate of 5 - 9 g/min. After spraying was complete the drug loaded cores were dried.

150 g of the dried cores were lubricated with 0.75 g Aerosil® (sifted through BSS #60 mesh) and sprayed with the prepared coating solution described in Table 5.2, as follows:

Table 5.2

Ingredient	Amount used (g)	Dry wt. (g)
Eudragit L30D	66.67	20.0
Carbomer (Aqueous Carbopol® 971P Dispersion 1% w/w)	40.0	0.40
Polyethylene glycol USNF (PEG 1500)	3.06	3.06
Lactose Monohydrate USNF	2.04	2.04
Talc USP (Aqueous Talc Dispersion 40% w/w)	51.0	20.4
Purified Water USP upto	200.0	--

The total polymer content of the applied coat was 11.90% by weight of the core while the total solids application was 27% by weight of the core. The bitter taste of ciprofloxacin was masked with the applied coat without affecting dissolution, as shown in Table 5.3

Table 5.3

Time (Min.)	Percent drug released 0.1N HCl; 75 rpm; 900ml, USP app-2	
	Uncoated	Coated
5.0	87.0	7.20
10.0	97.8	27.2
15.0	100.7	46.3
20.0	-	62.90
25.0	-	76.0
30.0	-	85.1

EXAMPLE 6

Table 6.1 describes another coating composition containing a film forming polymer (ethyl cellulose) and a swellable polymer (carbopol).

Table 6.1

Ingredient	Amount used (g)	Dry wt. (g)
Ethyl Cellulose Aqueous dispersion USNF (Aquacoat® ECD-30)	100.0	30.0
Carbomer	60.0	0.60

(Aqueous Carbopol® 971P Dispersion 1% w/w)		
Triethyl Citrate USNF	6.0	--
Talc USP (Aqueous Talc Dispersion 30% w/w)	30.0	9.0
Purified Water USP upto	200.0	--

To prepare the coating solution an aqueous talc dispersion (30% w/w) was added to a 1% carbopol dispersion in water under stirring for 30 minutes. The carbopol – talc dispersion was finally added into plasticized (with triethyl citrate) ethyl cellulose dispersion with stirring for 30-40 minutes.

Core containing Paracetamol were prepared using the formula described in Table 6.2.

Table 6.2

Ingredient	Amount used (g)
Paracetamol USP	260.0
Povidone USP (PVP K-30)	28.0
Lactose Monohydrate USNF	18.0
Microcrystalline cellulose USNF (Avicel® PH 101)	90.0
Colloidal Silicon Dioxide USNF (Aerosil® 200)	4.0

Total	400.0

Paracetamol, PVP K-30, Lactose, and Avicel PH 101 were mixed in a double cone blender for 10 minutes. They were then granulated with water, dried in a tray drier at 60°C for 4 hours and sifted to give BSS fraction #30/85. The granules thus obtained were lubricated with Aerosil 200 and sprayed with the prepared coating solution using Wurster Coater (Glatt GPCG–1, GmbH, Germany). The total polymer content of the coat applied was 12% by weight of the core. This coating effectively masked the pungent taste of paracetamol and also gave the desired dissolution profile as shown in Table 6.3

Table 6.3

Time (Min.)	**Percent drug released PH 5.8 Phosphate buffer; 50 rpm; 900ml**	
	Uncoated	**Coated**
5.0	90.1	23.7
10.0	97.7	62.4
15.0	97.9	88.0
20.0	98.1	98.2
25.0	98.3	98.9
30.0	98.4	99.3

EXAMPLE 7

Example 7 deals with the same coating composition as given in Table 6.1, wherein ethyl cellulose has been combined with carbopol in a 100 : 2 proportion. The drug particles which have been coated is constituted of ciprofloxacin base and its composition is described in Table 7.1.

Table 7.1

Ingredient	Amount used (g)
Ciprofloxacin USP	50.0
Lactose Monohydrate USNF	3.5
Povidone USP (PVP K-30)	5.5
Microcrystalline cellulose USNF (Avicel PH101)	17.5
Colloidal Silicon Dioxide USNF (Aerosil 200)	00.75
Total	77.25

Weighed amount of ciprofloxacin, lactose, Avicel PH 101 and PVP K-30 were sifted through BSS #44 and dry mixed in a double cone blender. The blend was granulated with sufficient water to form a cohesive mass. The wet mass was dried in a tray drier and sifted through BSS #30 and retained on BSS #85. The dried material was lubricated with sifted Aerosil (sieved through BSS #60) and then loaded

in Glatt GPCG-1 Wurster for coating with ethyl cellulose-carbopol solution (described in Table 6.1).

A total polymer application of 15% of the weight of the cores (total solids applied were 34.35%) was sufficient to mask the bitter taste of ciprofloxacin without affecting the dissolution significantly.

Table 7.2 shows the dissolution profiles of the coated and uncoated granules using USP apparatus - 2 at 75 rpm in 900 ml of 0.1N hydrochloric acid.

Table 7.2

Time (Min.)	Percent drug released 0.1N HCl, 75 rpm; 900ml, USP app-II	
	Uncoated	Coated
5.0	83.3	12.8
10.0	97.7	31.7
15.0	97.8	58.7
20.0	98.1	70.8
25.0	-	82.6
30.0	-	95.2

While the present invention has been described in terms of its specific embodiments, certain modifications and equivalents will be apparent to those skilled in the art and are intended to be included within the scope of the present invention.

WE CLAIM :

1 A coating composition, used for the film coating of pharmaceutical cores containing the drug, said composition comprising a suitable film forming material in combination with a high viscosity swellable polymer and optionally other suitable ingredients for coating including lubricants, plasticisers and channeling agents.

2. The composition of claim 1, wherein the film forming material comprises methacrylic acid copolymers, polymethacrylate-methylmethacrylate copolymers, alkyl celluloses or mixtures thereof.

3. The composition of claim 2, wherein the dry weight of the film forming polymer applied is upto a maximum of 30% of the weight of the core.

4. The composition of claim 1, wherein the high viscosity swellable polymer comprises carbopol, carragennan, polyvinyl alcohol, cellulosic polymers or other suitable high viscosity gums.

5. The composition of claim 4, wherein the swellable polymer is present from 0.1 to 20% w/w of the dry weight of film forming polymer.

6. The composition of claim 4, wherein high viscosity swellable polymer is carbopol.

7. The composition of claim 1, wherein channeling agents are included and are selected from the group consisting of lactose, starch, talc and mixtures thereof.

8. The composition of claim 7, wherein the channeling agent is present in an amount up to 100% of the dry weight of polymers.

9. The composition of claim 8, wherein the channeling agent is present in an amount up to 60% of the dry weight of polymers.

10. The composition of claim 9, wherein the channeling agent is present in an amount up to 30% of the dry weight of polymers.

11. The composition of claim 1, wherein the lubricants are present and are selected from the group consisting of talc, glyceryl monostrearate, magnesium stearate, colloidal silica and mixtures thereof.

12. The composition of claim 11, wherein the lubricant is present in an amount up to 200% of the dry weight of the film forming polymer.

13. The composition of claim 12, wherein the lubricant is present in an amount up to 100% of the dry weight of the film forming polymer.

14. The composition of claim 1, wherein the plasticisers are incorporated in the film and are selected from the group consisting of polyethylene glycol, acetylated

monoglycerides, glyceryl monostearate, glyceryl triacetate, acetyl triethylcitrate, triethylcitrate, dibutyl phthalate, dibutyl sebacate and mixtures thereof.

15. The composition of claim 14, wherein the plasticizer is present in an amount upto 40% of the dry weight of film forming polymer.

16. The composition of claim 15, wherein the plasticizer is polyethylene glycol (PEG).

17. The composition of claim 1, which includes 0.5 to 30% of the dry weight of the polymers by weight of the cores.

18. The composition of claim 14, wherein the coated particles are formulated as sprinkles, dry powder, liquitabs, suspension, emulsion, or as whole, chewable, or dispersible tablet, or any other suitable oral dosage forms.

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(54) Title: TASTE MASKING COATING COMPOSITIONS

(57) Abstract

A coating composition is described for the film coating of pharmaceutical cores containing the drug, said composition comprising a suitable film forming material in combination with a high viscosity swellable polymer.

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Declaration and Power of Attorney For Patent Application

English Language Declaration

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name,

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled

TASTE MASKING COATING COMPOSITIONS

the specification of which

(check one)

☐ is attached hereto.

☒ was filed on **26 October 1999** as United States Application No. or PCT International Application Number **PCT/IB99/01735**

and was amended on _____
(if applicable)

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose to the United States Patent and Trademark Office all information known to me to be material to patentability as defined in Title 37, Code of Federal Regulations, Section 1.56.

I hereby claim foreign priority benefits under Title 35, United States Code, Section 119(a)-(d) or Section 365(b) of any foreign application(s) for patent or inventor's certificate, or Section 365(a) of any PCT International application which designated at least one country other than the United States, listed below and have also identified below, by checking the box, any foreign application for patent or inventor's certificate or PCT International application having a filing date before that of the application on which priority is claimed.

Prior Foreign Application(s)			Priority Not Claimed
454/Del/1999	**India**	**19 March 1999**	☐
(Number)	(Country)	(Day/Month/Year Filed)	
(Number)	(Country)	(Day/Month/Year Filed)	☐
(Number)	(Country)	(Day/Month/Year Filed)	☐

I hereby claim the benefit under 35 U.S.C. Section 119(e) of any United States provisional application(s) listed below:

(Application Serial No.)	(Filing Date)
(Application Serial No.)	(Filing Date)
(Application Serial No.)	(Filing Date)

I hereby claim the benefit under 35 U. S. C. Section 120 of any United States application(s), or Section 365(c) of any PCT International application designating the United States, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT International application in the manner provided by the first paragraph of 35 U.S.C. Section 112, I acknowledge the duty to disclose to the United States Patent and Trademark Office all information known to me to be material to patentability as defined in Title 37, C. F. R., Section 1.56 which became available between the filing date of the prior application and the national or PCT International filing date of this application:

(Application Serial No.)	(Filing Date)	(Status) (patented, pending, abandoned)
(Application Serial No.)	(Filing Date)	(Status) (patented, pending, abandoned)
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I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

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